

SOME DERIVATIVES  
OF  
GELSEMINE

BY

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CXXXII.—*Some Derivatives of Gelsemine.*

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IN a recent communication (Trans., 1910, **97**, 2223) the author has described the isolation of the alkaloid gelsemine, in a pure state, from the rhizome and roots of *Gelsemium sempervirens*, Aiton, and has shown that it possesses the formula  $C_{20}H_{22}O_2N_2$ .

Apart from some of the salts of gelsemine, the only derivatives of the base that have previously been described are the methiodide and the hydrochlorides of the acetyl and benzoyl derivatives (Goeldner, *Ber. Deut. pharm. Ges.*, 1895, **5**, 330). Even these derivatives do not appear to have been obtained in a pure condition, as their analysis led Goeldner (*loc. cit.*) to the conclusion that the parent base possessed the formula  $C_{22}H_{26}O_3N_2$ , instead of  $C_{20}H_{22}O_2N_2$ , which the present author has shown to be the correct one.

A quantity of gelsemine being available, it appeared of interest to undertake an investigation of some derivatives of the alkaloid, as it was hoped that thereby some light might be thrown on its constitution. Although the amount of material at disposal did not suffice for extending our knowledge in this direction, a number of interesting derivatives have been prepared.

Attempts to obtain definite oxidation products from gelsemine were unsuccessful owing to the ease with which the alkaloid breaks down when acted on by oxidising agents. On the other hand, the base is very stable towards reducing agents, since it remains intact on boiling its alcoholic solution with sodium. A similar stability is shown towards alkali hydroxides.

On boiling gelsemine for some hours with concentrated hydrochloric acid, it has been found that three new bases are formed. The chief product of this reaction is an amorphous substance possessing the formula  $C_{20}H_{24}O_3N_2$ , and which corresponds, therefore, with gelsemine, to which the elements of one molecule of water have been added. It has been designated as *apogelsemine*, and several of its derivatives have been prepared. The other two bases which are formed together with *apogelsemine* possess the formulæ  $C_{20}H_{23}O_2N_2Cl$  and  $C_{20}H_{24}O_3N_2$  respectively, the latter being a hydrolytic product of the former. Both these bases crystallise readily, and have been designated as *chloroisoapogelsemine* and *isoapogelsemine* respectively. They and several of their derivatives have now been characterised.

It has further been observed that on heating gelsemine methiodide with potassium hydroxide, or *gelsemine methyl*

*hydroxide* with water, at about  $200^{\circ}$ , an anomalous change takes place, inasmuch as the expected gelsemethine is not formed, gelsemine being regenerated with the elimination of methyl alcohol.

The *methyl hydroxide* of apogelsemine behaves in an analogous manner, as on heating with water apogelsemine is regenerated.

### EXPERIMENTAL.

The gelsemine employed was isolated from the dried rhizome and roots of *Gelsemium sempervirens*, Aiton, in the manner previously described (*loc. cit.*).

The alkaloid crystallises from acetone in handsome, glistening prisms, melting at  $178^{\circ}$ , and has  $[\alpha]_D + 15.9^{\circ}$  in chloroform solution. As already mentioned, it possesses the empirical formula  $C_{20}H_{22}O_2N_2$ . It is monobasic, and its hydrochloride,



forms small, glistening prisms, melting at about  $300^{\circ}$ , and having  $[\alpha]_D + 2.6^{\circ}$  in aqueous solution.

Gelsemine is not attacked by even prolonged heating with potassium hydroxide solution or by treatment with sodium in boiling alcoholic solution. On the other hand, it is very readily oxidised by potassium permanganate, but no definite products have been obtained by this means. The alkaloid contains no methoxyl or ethoxyl group.

*Acetylgelsemine*,  $C_{20}H_{21}ON_2 \cdot OAc$ .—The presence of a hydroxyl group in gelsemine has already been shown by Goeldner (*loc. cit.*), who obtained the acetyl and benzoyl derivatives of the base in the form of their hydrochlorides. The acetylated base, however, has not previously been described.

A quantity (5 grams) of gelsemine was boiled for one hour with acetic anhydride (50 grams) in the presence of a trace of pyridine. The reaction mixture was then shaken with ice and water until a homogeneous liquid was obtained, after which the base was precipitated by sodium carbonate and extracted with ether.

*Acetylgelsemine* crystallises from methyl alcohol in large, colourless prisms, containing one molecule of the solvent, which melt indefinitely at  $60-70^{\circ}$ . The methyl alcohol of crystallisation is partly lost by exposure to the air, and completely on heating at  $100^{\circ}$ , after which the base melts at  $106-108^{\circ}$ :

0.3760,\* when heated at  $100^{\circ}$ , lost  $0.0295 CH_4O$ .  $CH_4O = 7.8$ .

0.1256 † gave  $0.3333 CO_2$  and  $0.0760 H_2O$ .  $C = 72.4$ ;  $H = 6.7$ .

0.1304 † „  $0.3460 CO_2$  „  $0.0778 H_2O$ .  $C = 72.3$ ;  $H = 6.7$ .

$C_{22}H_{24}O_3N_2 \cdot CH_4O$  requires  $CH_4O = 8.1$  per cent.

$C_{22}H_{24}O_3N_2$  requires  $C = 72.5$ ;  $H = 6.6$  per cent.

\* Air-dried.

† Dried at  $120^{\circ}$ .

0.3490,† made up to 20 c.c. with chloroform, gave  $\alpha_D + 0^\circ 50'$  in a 2-dcm. tube, whence  $[\alpha]_D + 23.9^\circ$ .

*Acetylgelsemine hydrochloride*,  $C_{20}H_{21}ON_2 \cdot OAc, HCl$ , was prepared by passing dry hydrogen chloride into an ethereal solution of the base. It crystallises readily, in small prisms, from a mixture of methyl alcohol and ethyl acetate:

0.1346 gave 0.0510 AgCl.  $Cl = 9.3$ .

$C_{22}H_{24}O_3N_2, HCl$  requires  $Cl = 8.8$  per cent.

*Gelsemine Methiodide*,  $C_{20}H_{22}O_2N_2, CH_3I$ .—This substance was first prepared by Goeldner (*loc. cit.*), but it was not correctly characterised by him. It crystallises from alcohol in large, handsome prisms, and from water in glistening leaflets containing one molecule of water of crystallisation:

0.6006,\* when heated at  $120^\circ$ , lost 0.0210  $H_2O$ .  $H_2O = 3.5$ .

0.1632 † gave 0.3250  $CO_2$  and 0.0790  $H_2O$ .  $C = 54.3$ ;  $H = 5.4$ .

0.2820 † „ 0.1420 AgI.  $I = 27.2$ .

$C_{21}H_{25}O_2N_2I, H_2O$  requires  $H_2O = 3.7$  per cent.

$C_{21}H_{25}O_2N_2I$  requires  $C = 54.3$ ;  $H = 5.4$ ;  $I = 27.4$  per cent.

0.2050,† made up to 20 c.c. with water, gave  $\alpha_D + 0^\circ 11'$  in a 2-dcm. tube, whence  $[\alpha]_D + 8.9^\circ$ .

With the object of obtaining the corresponding gelsemethine, a quantity (1 gram) of gelsemine methiodide was heated at  $200^\circ$  for some hours with about 25 c.c. of 20 per cent. aqueous potassium hydroxide. When cool, the alkaline liquid was acidified, filtered, rendered alkaline with sodium carbonate, and extracted with ether. A quantity of a substance was thus removed, which, after crystallisation from acetone, formed glistening prisms, melting at  $178^\circ$ , and was found to be gelsemine.

It is thus seen that gelsemine methiodide behaves in an anomalous manner on heating with potassium hydroxide, inasmuch as it does not yield the expected gelsemethine, but is deprived of methyl alcohol, the original base being regenerated.

For the preparation of *gelsemine methyl hydroxide*, the corresponding methiodide was treated with silver sulphate, and to the resulting methosulphate the requisite amount of barium hydroxide was added. After removing the barium sulphate, the strongly alkaline aqueous solution of the quaternary hydroxide was concentrated to the consistency of a syrup, but all attempts to isolate the methyl hydroxide in a crystalline condition were unsuccessful.

On heating an aqueous solution of gelsemine methyl hydroxide at  $220$ – $240^\circ$ , the base was found to undergo a change analogous to that shown above to occur when the corresponding methiodide

\* Air-dried.

† Dried at  $120^\circ$ .

is heated with aqueous potassium hydroxide, methyl alcohol being eliminated, with the regeneration of gelsemine.

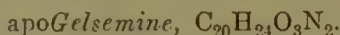
*The Action of Hydrochloric Acid on Gelsemine.*

Since alkali hydroxides and reducing agents had no action on gelsemine, the effect of heating the base with acids was investigated.

A quantity (10 grams) of gelsemine was boiled for about three hours with 100 c.c. of concentrated hydrochloric acid. The solution was then evaporated to dryness under diminished pressure, the last traces of water being removed by repeated evaporation with alcohol. The product was dissolved in a small quantity of boiling absolute alcohol, and boiling ethyl acetate was added to the solution until a slight turbidity was produced. On keeping, a crystalline product separated, which was collected, washed with ethyl acetate, and dried, when it amounted to between 8 and 9 grams. The product contained in the filtrate from the hydrochlorides could not be readily crystallised, and is referred to later.

The above-mentioned crystalline substance appeared homogeneous, and, on analysis, gave numbers corresponding with the formula  $C_{20}H_{26}O_4N_2.HCl$ , but on attempting to prepare the corresponding base, it was found to consist of a mixture of the hydrochlorides of three bases, which were separated as follows.

Five grams of the above-mentioned mixed hydrochlorides were dissolved in about 250 c.c. of 30 per cent. alcohol, and 0.7 gram of sodium carbonate, dissolved in water, was added to the hot solution. A current of steam was then passed through the mixture until all the alcohol was removed, when a crystalline substance separated. This was removed from the hot solution, and washed with a little boiling water, when it formed small, glistening prisms, in amounts varying from 0.5 to 0.8 gram.



The aqueous liquid from which the above-mentioned crystalline substance had been separated was extracted with chloroform, which removed a quantity of an amorphous base soluble in water. This was dissolved in a small quantity of acetone, and on inoculating the solution with *isoapogelsemine*, subsequently described, about 0.3 gram of the latter slowly separated.

The acetone solution from which the crystalline substance had been removed yielded about 3 grams of a base: this represents the chief product of the action of hydrochloric acid on gelsemine, and although the substance is amorphous, it was found to be homogeneous, and has been designated as *apogelsemine*.

*apoGelsemine* is a strongly basic substance, readily soluble in



hot water and most organic solvents with the exception of ether, in which it is only sparingly soluble. All attempts to obtain the base in a crystalline condition were unsuccessful.

*apoGelsemine Hydrochloride*,  $C_{20}H_{24}O_3N_2 \cdot HCl \cdot H_2O$ .—This salt was prepared by evaporating an aqueous solution of *apogelsemine* in dilute hydrochloric acid to dryness, and crystallising the residue from a mixture of alcohol and ethyl acetate. It forms colourless, glistening needles, melting indefinitely between  $250^\circ$  and  $260^\circ$ . After drying at  $115$ – $120^\circ$  it was analysed:

0.1805 gave 0.0660 AgCl.  $Cl = 9.0$ .

0.1432 „ 0.3176  $CO_2$  and 0.0919  $H_2O$ .  $C = 60.5$ ;  $H = 7.1$ .

0.1440 „ 0.3204  $CO_2$  „ 0.0920  $H_2O$ .  $C = 60.6$ ;  $H = 7.1$ .

0.2292 „ 14.0 c.c.  $N_2$  at  $26^\circ$  and 770 mm.  $N = 6.9$ .

$C_{20}H_{26}O_4N_2 \cdot HCl$  requires  $C = 60.8$ ;  $H = 6.8$ ;  $N = 7.1$ ;

$Cl = 9.0$  per cent.

From these figures *apogelsemine* would appear to have the formula  $C_{20}H_{26}O_4N_2$ , yielding the hydrochloride  $C_{20}H_{26}O_4N_2 \cdot HCl$ . It was found, however, from the analysis of the methiodide and the acetyl derivatives that the formula of the base is  $C_{20}H_{24}O_3N_2$ , the hydrochloride crystallising with one molecule of water, which is not lost on drying at  $120^\circ$ . Thus *apogelsemine* appears to be formed by the addition of the elements of one molecule of water to gelsemine.

A determination of the specific rotatory power of the hydrochloride gave the following result:

0.4142, made up to 20 c.c. with water, gave  $\alpha_D + 0^\circ 47'$  in a 2-dcm. tube, whence  $[\alpha]_D + 18.9^\circ$ .

*apoGelsemine Methiodide*,  $C_{20}H_{24}O_3N_2 \cdot CH_3I$ .—This derivative was prepared by the action of methyl iodide on a solution of *apogelsemine* in ethyl acetate. It crystallises in colourless prisms, melting and decomposing at about  $295^\circ$ :

0.1272 gave 0.2456  $CO_2$  and 0.0660  $H_2O$ .  $C = 52.6$ ;  $H = 5.7$ .

$C_{21}H_{27}O_3N_2I$  requires  $C = 52.3$ ;  $H = 5.6$  per cent.

0.2670, made up to 20 c.c. with water, gave  $\alpha_D + 0^\circ 20'$  in a 2-dcm. tube, whence  $[\alpha]_D + 12.4^\circ$ .

*apoGelsemine methyl hydroxide* was prepared in the manner described in connexion with gelsemine methyl hydroxide, but, like that substance, it could not be obtained in a crystalline condition.

With the endeavour to obtain the corresponding *apogelsemethine*, a quantity of *apogelsemine* methyl hydroxide was heated in aqueous solution for three hours at  $210^\circ$ . The liquid was then acidified, filtered, and the filtrate rendered alkaline with sodium carbonate, and extracted with chloroform. This removed a quantity of an amorphous base, which was found to be *apogelsemine*. since on

warming with methyl iodide it was converted into *apogelsemine* methiodide. (Found, C=52.5; H=6.0. Calc., C=52.3; H=5.6 per cent.) *apoGelsemine* methyl hydroxide behaves, therefore, in the same anomalous manner as *gelsemine* methyl hydroxide, inasmuch as by the above treatment methyl alcohol is eliminated and *apogelsemine* regenerated.

*Diacetyl**apogelsemine Hydrochloride*,  $C_{20}H_{22}ON_2(OAc)_2 \cdot HCl$ .—The presence of two hydroxyl groups in *apogelsemine* was shown by the formation of a diacetyl derivative. *apoGelsemine* (2 grams) was boiled for about two hours with acetic anhydride (25 grams) in the presence of a trace of pyridine. The solution was afterwards evaporated almost to dryness under diminished pressure, the residue dissolved in ether, and dry hydrogen chloride passed into the solution. A white precipitate was produced, which was collected, dried in a desiccator, and crystallised from absolute alcohol, when it was obtained in glistening plates, melting at  $286^{\circ}$ :

0.3154 gave 0.0940 AgCl. Cl=7.4.

0.1384 „ 0.3150  $CO_2$  and 0.0815  $H_2O$ . C=62.1; H=6.5.

$C_{24}H_{29}O_5N_2Cl$  requires C=62.5; H=6.3; Cl=7.7 per cent.

This substance is thus identified as the *hydrochloride* of *diacetyl**apogelsemine*. A determination of its specific rotatory power gave the following result:

0.2150, made up to 20 c.c. with water, gave  $\alpha_D + 0^{\circ}28'$  in a 2-dem. tube, whence  $[\alpha]_D + 21.7^{\circ}$ .

*Diacetyl**apogelsemine* was obtained from the hydrochloride, but it could not be crystallised.

*Monoacetyl**apogelsemine*,  $C_{20}H_{23}O_2N_2 \cdot OAc$ .—On boiling an aqueous alcoholic solution of *diacetyl**apogelsemine* with potassium carbonate for a few minutes, one acetyl group is removed with the formation of the monoacetyl derivative.

*Monoacetyl**apogelsemine* crystallises from methyl alcohol in small, glistening prisms, which melt at  $295$ — $298^{\circ}$ . The substance appears to crystallise with one molecule of methyl alcohol, but this is so readily lost on exposure to the air that an exact determination of its amount was not practicable:

0.1444 \* gave 0.3660  $CO_2$  and 0.0900  $H_2O$ . C=69.1; H=6.9.

$C_{22}H_{26}O_4N_2$  requires C=69.1; H=6.8 per cent.

*Chloroisoapogelsemine*,  $C_{20}H_{23}O_2N_2Cl$ .

As above mentioned, during the separation of the bases from the mixed hydrochlorides obtained by the action of hydrochloric acid on *gelsemine*, a small quantity (0.5 to 0.8 gram) of a substance

\* Dried at  $120^{\circ}$ .



was isolated, which differed from *apogelsemine* by its insolubility in hot water.

This substance crystallises from dilute alcohol or ethyl acetate in glistening prisms. It begins to decompose at about  $220^{\circ}$ , but shows no definite melting point:

0.1304 gave 0.3230  $\text{CO}_2$  and 0.0800  $\text{H}_2\text{O}$ .  $\text{C}=67.5$ ;  $\text{H}=6.8$ .

0.1382 „ 0.3416  $\text{CO}_2$  „ 0.0836  $\text{H}_2\text{O}$ .  $\text{C}=67.4$ ;  $\text{H}=6.7$ .

0.2485 „ 17.0 c.c.  $\text{N}_2$  at  $25^{\circ}$  and 782 mm.  $\text{N}=7.8$ .

0.2782 „ 0.1070  $\text{AgCl}$ .  $\text{Cl}=9.5$ .

$\text{C}_{20}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl}$  requires  $\text{C}=67.0$ ;  $\text{H}=6.4$ ;  $\text{N}=7.8$ ;  $\text{Cl}=9.9$  per cent.

This substance would thus appear to be a monochloro-derivative of *apogelsemine*, more particularly as it can be obtained by boiling *apogelsemine* with hydrochloric acid. On hydrolysis it does not, however, regenerate *apogelsemine*, but yields a crystalline isomeride of the latter. It would therefore appear probable that the chloro-derivative is not related directly to *apogelsemine*, but to the new crystalline isomeride. It is therefore proposed to designate it as *chloroisoapogelsemine*, its hydrolytic product being named *isoapogelsemine*.

A determination of its specific rotatory power gave the following result:

0.2448, made up to 20 c.c. with chloroform, gave  $\alpha_D +1^{\circ}49'$  in a 2-dcm. tube, whence  $[\alpha]_D +74.2^{\circ}$ .

*Chloroisoapogelsemine Aurichloride*,  $\text{C}_{20}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl} \cdot \text{HAuCl}_4 \cdot \text{H}_2\text{O}$ .—This salt crystallises from dilute alcohol in orange prisms, which decompose at  $160^{\circ}$ , and appear to retain a molecule of water which is not lost at  $120^{\circ}$ :

0.1820 gave 0.0494 Au.  $\text{Au}=27.1$ .

$\text{C}_{20}\text{H}_{24}\text{O}_2\text{N}_2\text{Cl}_5\text{Au} \cdot \text{H}_2\text{O}$  requires  $\text{Au}=27.5$  per cent.

*Chloroisoapogelsemine Methiodide*,  $\text{C}_{20}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl} \cdot \text{CH}_3\text{I}$ .—This substance was prepared by the action of methyl iodide on an alcoholic solution of *chloroisoapogelsemine*. It crystallises from methyl alcohol in glistening prisms, melting and decomposing at about  $265^{\circ}$ :

0.1485 gave 0.2750  $\text{CO}_2$  and 0.0740  $\text{H}_2\text{O}$ .  $\text{C}=50.5$ ;  $\text{H}=5.5$ .

$\text{C}_{21}\text{H}_{26}\text{O}_2\text{N}_2\text{ClI}$  requires  $\text{C}=50.3$ ;  $\text{H}=5.2$  per cent.

*Chloroacetylisoapogelsemine*,  $\text{C}_{20}\text{H}_{22}\text{ON}_2\text{Cl} \cdot \text{OAc}$ .—*Chloroisoapogelsemine* was dissolved in about ten times its weight of acetic anhydride, and, after the addition of a drop of pyridine, the solution was boiled for two hours. The reaction mixture was then poured into water, the base precipitated by means of sodium carbonate, and extracted with chloroform. *Chloroacetylisoapogelsemine* crystal-

lises from methyl alcohol in small, colourless prisms, melting at  $180^{\circ}$ :

0.1340 gave 0.3234  $\text{CO}_2$  and 0.0770  $\text{H}_2\text{O}$ .  $\text{C} = 65.8$ ;  $\text{H} = 6.4$ .

$\text{C}_{22}\text{H}_{25}\text{O}_3\text{N}_2\text{Cl}$  requires  $\text{C} = 65.9$ ;  $\text{H} = 6.2$  per cent.

0.2040, made up to 20 c.c. with chloroform, gave  $\alpha_D + 2^{\circ}55'$  in a 2-dem. tube, whence  $[\alpha]_D + 142.9^{\circ}$ .

#### *Action of Diethylaniline on Chloroisapogelsemine.*

If chloroisapogelsemine be boiled with diethylaniline for a short time it loses the elements of hydrochloric acid with the formation of a base which appears to be an isomeride of gelsemine.

One gram of chloroisapogelsemine was dissolved in 10 grams of diethylaniline, and the solution boiled for about ten minutes. Aqueous sodium carbonate was then added to the mixture, and the diethylaniline removed by distilling in a current of steam. On extracting the aqueous liquid with ether, and removing the solvent, a base was obtained which crystallised from acetone in glistening prisms, melting at  $105\text{--}108^{\circ}$ .

The air-dried crystals contain one molecule of acetone, which is lost on heating at  $100^{\circ}$ , the base then melting at  $140\text{--}145^{\circ}$ :

0.1388,\* when heated at  $100^{\circ}$ , lost 0.0210  $\text{C}_3\text{H}_6\text{O}$ .  $\text{C}_3\text{H}_6\text{O} = 15.1$ .

0.1188 † gave 0.3224  $\text{CO}_2$  and 0.0752  $\text{H}_2\text{O}$ .  $\text{C} = 74.0$ ;  $\text{H} = 7.0$ .

$\text{C}_{20}\text{H}_{22}\text{O}_2\text{N}_2, \text{C}_3\text{H}_6\text{O}$  requires  $\text{C}_3\text{H}_6\text{O} = 15.3$  per cent.

$\text{C}_{20}\text{H}_{22}\text{O}_2\text{N}_2$  requires  $\text{C} = 74.5$ ;  $\text{H} = 6.8$  per cent.

0.1192, † made up to 20 c.c. with chloroform, gave  $\alpha_D + 0^{\circ}18'$  in a 2-dem. tube, whence  $[\alpha]_D + 25.2^{\circ}$ .

The substance is therefore isomeric with gelsemine, differing from the latter in its melting point and its specific rotatory power. The melting point, however, does not fall when the substance is mixed with gelsemine, so that it is conceivable that the preparation may be a mixture of gelsemine and an isomeride. The quantity of material available did not permit of its further examination.

*Bromoisapogelsemine*,  $\text{C}_{20}\text{H}_{23}\text{O}_2\text{N}_2\text{Br}$ .—If gelsemine is boiled for some hours with hydrobromic acid, a small yield (15 per cent.) of a *bromoisapogelsemine* is obtained, together with the above-described mixture of *apo*- and *isapo*-gelsemine.

*Bromoisapogelsemine* crystallises from ethyl acetate in glistening plates. Like the corresponding chloro-derivative, it begins to decompose at about  $220^{\circ}$ , but shows no definite melting point:

0.1263 gave 0.2790  $\text{CO}_2$  and 0.0676  $\text{H}_2\text{O}$ .  $\text{C} = 60.0$ ;  $\text{H} = 5.9$ .

0.1032 „ 0.0486  $\text{AgBr}$ .  $\text{Br} = 20.0$ .

$\text{C}_{20}\text{H}_{23}\text{O}_2\text{N}_2\text{Br}$  requires  $\text{C} = 59.6$ ;  $\text{H} = 5.7$ ;  $\text{Br} = 19.8$  per cent.

\* Air-dried.

† Dried at  $100^{\circ}$ .

The quantity of material available did not suffice for its further examination.

*isoapoGelsemine*,  $C_{20}H_{24}O_3N_2$ .

It has already been stated that, on crystallising the mixed hydrochlorides obtained by the action of hydrochloric acid on gelsemine, only about 80 per cent. of the product was readily obtained in a crystalline condition. The material contained in the filtrate from the crystalline hydrochlorides was therefore dissolved in water, excess of sodium carbonate added, and the base extracted with a large volume of chloroform. On concentrating the chloroform solution, a substance separated from the boiling liquid in small, colourless prisms, melting at about  $290-300^\circ$ . This compound was found to be identical with that obtained by the hydrolysis of chloro*isoapogelsemine*, and has been designated as *isoapogelsemine*. After recrystallisation from alcohol, the melting point became constant at about  $310^\circ$ :

0.1390 gave 0.3614  $CO_2$  and 0.0920  $H_2O$ .  $C=70.9$ ;  $H=7.3$ .

0.1408 „ 0.3641  $CO_2$  „ 0.0920  $H_2O$ .  $C=70.5$ ;  $H=7.2$ .

0.2432 „ 17.0 c.c.  $N_2$  at  $26^\circ$  and 764 mm.  $N=7.8$ .

$C_{20}H_{24}O_3N_2$  requires  $C=70.6$ ;  $H=7.1$ ;  $N=8.2$  per cent.

0.4812, made up to 20 c.c. with pyridine, gave  $\alpha_D + 0^\circ 48'$  in a 2-dcm. tube, whence  $[\alpha]_D + 16.6^\circ$ .

*isoapoGelsemine* is almost insoluble in most solvents, with the exception of pyridine, in which it dissolves fairly readily.

*isoapoGelsemine Hydrochloride*,  $C_{20}H_{24}O_3N_2 \cdot HCl \cdot H_2O$ .—This salt was prepared in the same manner as *apogelsemine hydrochloride*. Like the latter, it retains one molecule of water of crystallisation, which is not lost on heating at  $120^\circ$ :

0.1200 gave 0.2656  $CO_2$  and 0.0788  $H_2O$ .  $C=60.4$ ;  $H=7.3$ .

$C_{20}H_{25}O_3N_2Cl \cdot H_2O$  requires  $C=60.8$ ;  $H=6.8$  per cent.

0.2090, made up to 20 c.c. with water, gave  $\alpha_D + 0^\circ 34'$  in a 2-dcm. tube, whence  $[\alpha]_D + 27.1^\circ$ .

*isoapoGelsemine Methiodide*,  $C_{20}H_{24}O_3N_2 \cdot CH_3I$ .—This substance was formed by the action of methyl iodide on *isoapogelsemine* in alcoholic solution. It crystallises from methyl alcohol in glistening plates, melting and decomposing at  $266^\circ$ :

0.2445 gave 0.1180  $AgI$ .  $I=26.0$ .

$C_{21}H_{27}O_3N_2I$  requires  $I=26.3$  per cent.

A determination of its specific rotatory power gave the following result:

0.3260, made up to 20 c.c. with water, gave  $\alpha_D + 0^\circ 55'$  in a 2-dcm. tube, whence  $[\alpha]_D + 28.1^\circ$ .

*Diacetylisopogelsemine Hydrochloride*,  $C_{20}H_{22}ON_2(OAc)_2 \cdot HCl$ .—This derivative was prepared in the same manner as the above-described diacetyl*pogelsemine* hydrochloride. Unlike the latter compound, it is very sparingly soluble in boiling absolute alcohol, but dissolves readily in hot 95 per cent. alcohol, separating in glistening plates, which contain one molecule of water of crystallisation, and melt at  $305^\circ$ :

0.1460 gave 0.3236  $CO_2$  and 0.0870  $H_2O$ .  $C = 60.4$ ;  $H = 6.6$ .

0.2706 „ 0.0810  $AgCl$ .  $Cl = 7.4$ .

$C_{24}H_{29}O_5N_2Cl \cdot H_2O$  requires  $C = 60.2$ ;  $H = 6.4$ ;  $Cl = 7.4$  per cent.

0.2304, made up to 20 c.c. with water, gave  $\alpha_D + 0.34'$  in a 2-dem. tube, whence  $[\alpha]_D + 24.6^\circ$ .

*Diacetylisopogelsemine* was prepared from its hydrochloride, but could not be crystallised. No monoacetyl derivative could be obtained from it.

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